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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/890,167	07/27/2001	Nancy L. Paiva	11137/04704	7718

7590 09/24/2004

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EXAMINER

KRUSE, DAVID H

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 09/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	09/890,167	PAIVA ET AL.
	<b>Examiner</b>	<b>Art Unit</b>
	David H Kruse	1638

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 14 June 2004.  
 2a) This action is **FINAL**.      2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-18 and 21-67 is/are pending in the application.  
 4a) Of the above claim(s) 31-33 is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 1-18,21-30,34-42 and 58-67 is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____. | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
|   | 6) <input type="checkbox"/> Other: _____.                                   |

### **DETAILED ACTION**

1. This Office action is supplemental to the Office action mailed 2 September 2004. Consequently the shortened statutory period for reply has been reset upon mailing of this Office action.
2. Those rejections not specifically addressed in this Office action are withdrawn in view of Applicant's amendments to the claims.
3. The rejection of claims 1, 2, 15, 16, 24-27, 29, 34, 39, 41 and 67 under 35 U.S.C. § 102(b) as being anticipated by Leekband and Lorz is withdrawn in view of Applicant's arguments.
4. Claims 31-33 remain withdrawn from further consideration pursuant to 37 CFR § 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 5 November 2002.
5. This application contains claims 31-33 drawn to an invention nonelected without traverse in the reply filed on 5 November 2002. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR § 1.144) See MPEP § 821.01.
6. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

#### ***Claim Rejections - 35 USC § 112***

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-5, 8-12, 15-18, 21, 24-30, 34-36, 39-42, 58, 61, 64 and 67 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for edible plant material or edible plant comprising a transgenic plant cell transformed with a resveratrol synthase gene under the control of a constitutive promoter wherein said transgenic plant cell is a alfalfa or a soybean plant cell, and methods of making same, does not reasonably provide enablement for any transgenic plant cell transformed with a resveratrol synthase gene under the control of a constitutive promoter wherein said edible plant material or edible plant exhibits an increased concentration of resveratrol glucoside. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant claims edible plant material comprising transgenic plant cells transformed with a resveratrol synthase transgene under the control of a constitutive promoter whereby said transgenic plant cells accumulate resveratrol glucoside upon expression of said resveratrol synthase transgene, wherein said edible plant material exhibits an increased concentration of resveratrol glucoside as compared to edible plant material consisting of non-transgenic plant cells of the same cell type grown under the same conditions. Applicant also claims edible plants comprising said transgenic plant cells, and methods of making said edible plants comprising said transgenic plant cells.

Applicant teaches transgenic alfalfa and soybean plants transformed with a nucleic acid encoding a peanut resveratrol synthase under control of a constitutive promoter (CaMV 35S). See pages 20-24 and 32-34 of the Specification.

Applicant does not teach other transgenic plants transformed with a nucleic acid encoding a peanut resveratrol synthase under control of a constitutive promoter wherein said transgenic plant exhibits an increased concentration of resveratrol glucoside.

*In re Wands*, 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988) lists eight considerations for determining whether or not undue experimentation would be necessary to practice an invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claims.

Applicant states that one of skill in the art would not reasonably expect that a plant that does not naturally produce resveratrol would possess an endogenous glucosyl transferase capable of acting upon resveratrol to produce resveratrol glucoside (paragraph spanning pages 14-15 of the Response filed 14 June 2004). Applicant has only provided guidance for producing resveratrol glucoside in alfalfa and soybean by transforming with a resveratrol synthase gene operably linked to a constitutive promoter. Applicant provides no guidance on how one of skill in the art would recognize a plant that does not naturally produce resveratrol, but would possess an endogenous glucosyl transferase capable of acting upon resveratrol to produce resveratrol glucoside

without undue trial and error experimentation. See *In re Fisher*, 166 USPQ 18, 24 (CCPA 1970) which teaches “That paragraph (35 USC 112, first) requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art. In cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.”.

Claims 27, 34 and 41, which comprise a cultivating step wherein said transgenic plant cell is allowed to accumulate the precursors of resveratrol and minimize the concentration of  $\beta$ -glucosidase activity, lack adequate enablement. The instant claims require a cultivation step that is not adequately taught in the instant specification by which one of skill in the art would be able to use the claimed methods as broadly claimed. The specification states “Accumulation of RGluc is favored in plant tissues which contain the necessary biosynthetic precursors and low levels of  $\beta$ -glucosidases. Such conditions may be found in any plant cell, but are more likely to be present in non-stressed tissues, such as leaves constantly expressing RS driven by a constitutive promoter, rather than wounded or infected tissues which contain, release, or induce  $\beta$ -glucosidases” (page 18, 2<sup>nd</sup> paragraph of the specification). This general statement does not teach how to use the methods of the instant claims, only suggests that

wounding and/or infecting be avoided. The specification does not teach an active method of minimizing the concentration of  $\beta$ -glucosidase activity in a transgenic plant.

9. Claims 27, 34 and 41 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claimed methods comprise a cultivating step wherein said transgenic plant cell is allowed to accumulate the precursors of resveratrol and minimize the concentration of  $\beta$ -glucosidase activity. The instant specification does not teach the metes and bounds of such a cultivation step, and the instant claims do not recite any specific cultivating step that would achieve this limitation.

***Claim Rejections - 35 USC § 102***

10. Claims 1, 2, 8, 9, 15, 16, 24-27, 34, 39, 41 and 67 are rejected under 35 U.S.C. § 102(b) as being anticipated by Fischer (December 1994, Doctoral Dissertation, "Optimierung der heterologen Expression von Stilbensynthasegenen fur den Pflanzenschutz", Institut fiir Biotechnologie des Geschäftsbereichs Pflanzenschutz der Bayer AG, Leverkusen, an English translation by the Office of pages 106-115 is attached hereto) taken with the evidence of Kobayashi et al (2000, Plant Cell Reports Vol. 19, pages 904-910).

Fischer discloses a tobacco plant transformed with a nucleic acid encoding the peanut resveratrol synthase enzyme, operably linked to a 35S constitutive promoter (page 2 of the Translation). Fischer discloses that the transformed tobacco plant constitutively expresses the resveratrol synthase enzyme and produces resveratrol

(pages 4-5 of the Translation). Fischer discloses progeny plants of the transformed tobacco plant (see page 5 of the Translation). Fischer discloses that the transformed tobacco plant has increased disease resistance (see page 5 of the Translation). Without evidence to the contrary, the transformed tobacco plant of Fischer would inherently also produce resveratrol glucosides, because all plants inherently have 3-O-glucosyltransferases. Kobayashi *et al* disclose that a plant transformed with a nucleic acid encoding the peanut resveratrol synthase enzyme, operably linked to a 35S constitutive promoter produces the resveratrol-glucoside piceid (see Abstract on page 904). The methods at claims 27, 34, 39 and 41 are inherently disclosed by the disclosure of Fischer because there are not distinct manipulative method steps that distinguish the instant claimed methods from that disclosed by Fischer. See *Integra LifeSciences I Ltd. V. Merck KGaA* 50 USPQ2d 1846, 1850 (DC SCalf 1999), which teaches that where the prior art teaches all of the required steps to practice the claimed method and no additional manipulation is required to produce the claimed result, then the prior art anticipates the claimed method. The cultivating steps at claims 34 and 41 do not distinguish the claimed methods from that disclosed by Fischer.

***Claim Rejections - 35 USC § 103***

11. Claims 3-7, 10-14, 17, 18, 21-26, 28-30, 35-38, 40, 42 and 58-66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schroder *et al* (U.S. Patent 5,689,046 issued 18 November 1997) in view of Fischer (December 1994, Doctoral Dissertation) and further in view of Tropf *et al* (1994, J. Mol. Evol. 38:610-618).

The teachings of Schroder *et al* and Tropf *et al* can be found in a previous Office action.

The teachings of Fischer can be found above.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the teachings of Schroder *et al* to use the nucleic acid taught by Tropf *et al* encoding the amino acid sequence of Applicant's SEQ ID NO: 2, operably linked to a constitutive promoter as taught by Fischer to make a transgenic, edible plant material that produces resveratrol glucosides, especially piceid, such edible plant material not naturally producing resveratrol. Given the success of Fischer in constitutively expressing the peanut resveratrol synthase in tobacco, one of ordinary skill in the art would have had a reasonable expectation of success. The "use" of the edible plant material of the instant claims does not distinguish the invention from that taught by the prior art.

12. Claims 1-18, 21-30, 34-42 and 58-67 remain rejected under 35 U.S.C. § 103(a) as being unpatentable over Schroder *et al* (U.S. Patent 5,689,046 issued 18 November 1997) in view of Comai *et al* (U.S. Patent 5,106,739) and further in view of Tropf *et al* (1994, J. Mol. Evol. 38:610-618), Leekband and Lorz (Theoretical and Applied Genetics June 1998, 96:1004-1012) and Applicant's admission. This rejection is repeated for the reason of record as set forth in the last Office action mailed 10 March 2004. Applicant's arguments filed 14 June 2004 have been fully considered but they are not persuasive.

Withdrawn claims 31-33 were improperly included in this rejection in the previous Office action.

Applicant argues that there is no motivation or suggestion to combine the resveratrol transgene taught by Schroder with the promoter taught by Comai and the previous Office Action failed to identify where Schroder or Comai even suggest the desirability of constitutively expressing the resveratrol synthase gene in a plant, let alone the functionality of the combination (page 13, 2<sup>nd</sup> paragraph of the Response). Applicant further argues that the motivation to combine references must be found in the cited prior art or in the knowledge generally available to one of skill in the art, not in Applicants' specification and that the Action cannot piece together the prior art based on the teaching of Applicants to arrive at the hindsight conclusion that the claimed invention is obvious (page 13, 3<sup>rd</sup> paragraph of the Response). In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In the instant case the Examiner has demonstrated that use of constitutive promoters, such as that taught by Comai, to overexpress a protein (i.e. an enzyme) encoded by a transgene would have been obvious to one of ordinary skill in the art at the time of Applicant's invention. In the instant case the art readily recognized the function of both the resveratrol synthase transgene and the constitutive CaMV 35S promoter. Motivation to combine references

may be found without “something specific in a prior reference which would lead an inventor to combine the teachings therein with another piece of art”. See *Ex parte Anderson*, (BdPatApp&Int) 30 USPQ2d 1866 (9/14/1993), at 1868.

Applicant argues that Schroder, as suggesting the use of other promoter sequences operably linked to the resveratrol synthase, is vague and fails to provide the requisite motivation (page 14, 1<sup>st</sup> paragraph of the Response). This argument is addressed above.

Applicant argues that the cited art is deficient, as a basis for concluding that one of skill in the art would have a reasonable expectation that a resveratrol synthase transgene could be successfully expressed in a plant from a constitutive promoter to accumulate resveratrol glucoside. Applicant further argues that the complexity of successfully introducing and expressing a given coding sequence, particularly with heterologous combinations of expression elements not found in nature, an expectation of success in expressing a resveratrol synthase gene from a heterologous constitutive promoter would have been absent but for the teaching of Applicants' disclosure (page 14, 2<sup>nd</sup> paragraph of the Response). This argument is not found to be persuasive because the instant claims do not recite any materially different process step or element required to practice the claimed invention. As previously stated by the Examiner in the previous Office action, that the art teaches that it is desirable to introduce the resveratrol synthase gene into alfalfa and soybean as exemplified by Applicant and that in such an instance, the alfalfa or soybean would naturally produce resveratrol glucoside without further manipulation by one of ordinary skill in the art, and alfalfa and soybean were well

know in the art at the time of Applicant's invention as a desirable edible plant materials for both humans and animals.

Applicant argues that one of skill in the art would not have had a reasonable expectation that transgenic plant cells would accumulate resveratrol glucoside upon expression of the constitutively expressed resveratrol synthase transgene. Applicant argues that the resveratrol synthase gene produces resveratrol, not resveratrol glucoside and that the conversion of resveratrol to resveratrol glucoside is catalyzed by a glucosyl transferase. Applicant argues that one of ordinary skill in the art would not reasonably expect that a plant that does not naturally produce resveratrol would possess an endogenous glucosyl transferase capable of acting upon resveratrol to produce resveratrol glucoside (paragraph spanning pages 14-15 of the Response). These arguments are not found to be persuasive for the reasons given supra. The instant claims do not teach a manipulative step that would distinguish the invention from that suggested by the prior art and that would have been obvious to one of ordinary skill in the art at the time of the invention. If the plant requires a special inherent feature to have the claimed property, then the claims should be limited to such a plant or plants.

Applicant argues that to establish a *prima facie* case of obviousness, there must be a reasonable expectation of success and that the present rejection appears to rely on an "obvious to try" rationale, which is prohibited by the Federal Circuit (page 15, 2<sup>nd</sup> paragraph of the Remarks). This argument is not found to be persuasive because it is the Examiner's opinion that it would have been obvious to do not obvious to try. The art has established that it would have been obvious to introduce a resveratrol synthase

transgene into a soybean or alfalfa plant. The use of the constitutive promoter would have been obvious to use in view of the teachings of the art and the knowledge of one of ordinary skill in the art at the time of Applicant's invention. The fact that the art would have a different intended use than that of Applicant does not distinguish the claimed invention in the instant case.

Applicant argues that the claimed invention provided unexpected results that are of a significant, practical advantage and that a greater than expected result is a factor pertinent to the legal conclusion of obviousness MPEP § 716.02(a) (page 15, 2<sup>nd</sup> paragraph of the Remarks). This argument is not found to be persuasive because Applicant has not provided any affidavit or declaration to provide evidence of this assertion (MPEP § 716.02(b)). Applicant has provided no evidence that one of ordinary skill in the art would not have expected a transgenic plant to convert resveratrol to resveratrol glucoside if such a plant does not naturally produce resveratrol.

See *In re Lindner*, 173 USPQ 356 (CCPA 1972) and *In re Grasselli*, 218 USPQ 769 (Fed. Cir. 1983) which teach that the evidence of nonobviousness should be commensurate with the scope of the claims.

***Conclusion***

13. This Office action is supplemental to the Office action mailed 2 September 2004 and is non-final in view of the new grounds of rejection.
14. No claims are allowed.
15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David H. Kruse, Ph.D. whose telephone number is (571) 272-0799. The examiner can normally be reached on Monday to Friday from 8:00 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Amy Nelson can be reached at (571) 272-0804. The fax telephone number for this Group is (703) 872-9306 Before Final or (703) 872-9307 After Final.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group Receptionist whose telephone number is (571) 272-0547.



DAVID H. KRUSE, PH.D.  
PATENT EXAMINER

David H. Kruse, Ph.D.  
20 September 2004

16. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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